# RAW SEQUENCE LISTING
# ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/996,292

Source: OIPE

Date Processed by STIC: 12/6/01

**THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.**
**PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:**
1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**
**FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.**

**FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216.**
PATENTIN 2.1 e-mail help: patin21help@uspto.gov or phone 703-306-4119 (R. Wax)
PATENTIN 3.0 e-mail help: patin3help@uspto.gov or phone 703-306-4119 (R. Wax)

**TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 3.0 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW:**

## Checker Version 3.0

The Checker Version 3.0 application is a state-of the-art Windows based software program employing a logical and intuitive user-interface to check whether a sequence listing is in compliance with format and content rules. Checker Version 3.0 works for sequence listings generated for the original version of 37 CFR §§1.821 – 1.825 effective October 1, 1990 (old rules) and the revised version (new rules) effective July 1, 1998 as well as World Intellectual Property Organization (WIPO) Standard ST.25.
Checker Version 3.0 replaces the previous DOS-based version of Checker, and is Y2K-compliant. Checker allows public users to check sequence listings in Computer Readable form (CRF) before submitting them to the United States Patent and Trademark Office (USPTO).
Use of Checker prior to filing the sequence listing is expected to result in fewer errored sequence listings, thus saving time and money.

Checker Version 3.0 can be down loaded from the USPTO website at the following address:
**http://www.uspto.gov/web/offices/pac/checker**

## BEST AVAILABLE COPY

# Raw Sequence Listing Error Summary

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**ERROR DETECTED**      **SUGGESTED CORRECTION**      SERIAL NUMBER: 09|996, 292

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

1 ____ Wrapped Nucleics    The number/text at the end of each line "wrapped" down to the next line. This may occur if your file
        Wrapped Aminos ·   was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will
                           prevent "wrapping."

2 ____ Invalid Line Length   The rules require that a line not exceed 72 characters in length. This includes white spaces.

3 ____ Misaligned Amino    The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers;
        Numbering          use space characters, instead.

4 ____ Non-ASCII           The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please
                           ensure your subsequent submission is saved in ASCII text.

5 ____ Variable Length     Sequence(s)____contain n's or Xaa's representing more than one residue. Per Sequence Rules,
                           each n or Xaa can only represent a single residue. Please present the maximum number of each
                           residue having variable length and indicate in the <220>-<223> section that some may be missing.

6 ____ PatentIn 2.0        A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid
        "bug"              sequences(s) ____. Normally, PatentIn would automatically generate this section from the
                           previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to
                           the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for
                           Artificial or Unknown sequences.

7 ____ Skipped Sequences   Sequence(s) ____ missing. If intentional, please insert the following lines for each skipped sequence:
        (OLD RULES)        (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
                           (i)      SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
                           (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
                           This sequence is intentionally skipped

                           Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.

8 ____ Skipped Sequences   Sequence(s) ____ missing. If intentional, please insert the following lines for each skipped sequence.
        (NEW RULES)        <210> sequence id number
                           <400> sequence id number
                           000

9 ____ Use of n's or Xaa's   Use of n's and/or Xaa's have been detected in the Sequence Listing.
        (NEW RULES)        Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.
                           In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.

10 ____ Invalid <213>      Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or
        Response           scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or
                           is Artificial Sequence

11 ✓ Use of <220>         Sequence(s) ‾most‾ missing the <220> "Feature" and associated numeric identifiers and responses.
                           Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or
                           "Unknown." Please explain source of genetic material in <220> to <223> section.
                           (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32)  (Sec. 1.823 of Sequence Rules)

12 ____ PatentIn 2.0       Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file,
        "bug"              resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence
                           listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.

AMC – Biotechnology Systems Branch – 06/04/2001

OIPE

RAW SEQUENCE LISTING
PATENT APPLICATION:  US/09/996,292

DATE: 12/06/2001
TIME: 11:33:45

**Does Not Comply**
**Corrected Diskette Needed**

Input Set : A:\ISIS4804.ST25.txt
Output Set: N:\CRF3\12062001\I996292.raw

```
       3  <110> APPLICANT: Manoharan, Muthiah
       5  <120> TITLE OF INVENTION: Nuclease Resistant Chimeric Oligonucleotides
       7  <130> FILE REFERENCE: ISIS-4804
C-->   9  <140> CURRENT APPLICATION NUMBER: US/09/996,292
C-->   9  <141> CURRENT FILING DATE: 2001-11-28
       9  <160> NUMBER OF SEQ ID NOS: 55
      11  <170> SOFTWARE: PatentIn version 3.1
      13  <210> SEQ ID NO: 1
      14  <211> LENGTH: 20
      15  <212> TYPE: DNA
      16  <213> ORGANISM: Artificial Sequence
      18  <220> FEATURE:
      19  <223> OTHER INFORMATION: Novel Sequence
      21  <220> FEATURE:
      22  <221> NAME/KEY: misc_feature
      23  <222> LOCATION: (1)..(20)
      24  <223> OTHER INFORMATION: All P=S
      27  <220> FEATURE:
      28  <221> NAME/KEY: misc_feature
      29  <222> LOCATION: (1)..(1)
      30  <223> OTHER INFORMATION: N= L-Thymidine
      33  <220> FEATURE:
      34  <221> NAME/KEY: misc_feature
      35  <222> LOCATION: (20)..(20)
      36  <223> OTHER INFORMATION: N= L-Thymidine
      39  <400> SEQUENCE: 1
W-->  40  ngcatccccc aggccaccan                                          20
      43  <210> SEQ ID NO: 2
      44  <211> LENGTH: 17
      45  <212> TYPE: DNA
      46  <213> ORGANISM: Artificial Sequence
      48  <220> FEATURE:
      49  <223> OTHER INFORMATION: Novel Sequence
      51  <220> FEATURE:
      52  <221> NAME/KEY: misc_feature
      53  <222> LOCATION: (1)..(17)
      54  <223> OTHER INFORMATION: All P=S
      57  <220> FEATURE:
      58  <221> NAME/KEY: misc_feature
      59  <222> LOCATION: (1)..(1)
      60  <223> OTHER INFORMATION: N= L-Thymidine
      63  <220> FEATURE:
      64  <221> NAME/KEY: misc_feature
      65  <222> LOCATION: (2)..(3)
      66  <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
      69  <220> FEATURE:
      70  <221> NAME/KEY: misc_feature
```

The type of errors shown exist throughout the Sequence Listing. Please check subsequent sequences for similar errors.

- invalid response, see error summary sheet, item 11
(must explain source of genetic material)

RAW SEQUENCE LISTING                    DATE: 12/06/2001
PATENT APPLICATION:  US/09/996,292      TIME: 11:33:45

Input Set : **A:\ISIS4804.ST25.txt**
Output Set: **N:\CRF3\12062001\I996292.raw**

```
      71 <222> LOCATION: (15)..(15)
      72 <223> OTHER INFORMATION: N= 2'-O-MOE A
      75 <220> FEATURE:
      76 <221> NAME/KEY: misc_feature
      77 <222> LOCATION: (16)..(16)
      78 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
      81 <220> FEATURE:
      82 <221> NAME/KEY: misc_feature
      83 <222> LOCATION: (17)..(17)
      84 <223> OTHER INFORMATION: N= L-Thymidine
      87 <400> SEQUENCE: 2
W-->  88 nnncgctgtg atgcnnn                                      17
      91 <210> SEQ ID NO: 3
      92 <211> LENGTH: 20
      93 <212> TYPE: DNA
      94 <213> ORGANISM: Artificial Sequence
      96 <220> FEATURE:
      97 <223> OTHER INFORMATION: Novel Sequence
      99 <220> FEATURE:
     100 <221> NAME/KEY: misc_feature
     101 <222> LOCATION: (1)..(20)
     102 <223> OTHER INFORMATION: All P=S
     105 <220> FEATURE:
     106 <221> NAME/KEY: misc_feature
     107 <222> LOCATION: (1)..(1)
     108 <223> OTHER INFORMATION: N= L-Thymidine
     111 <220> FEATURE:
     112 <221> NAME/KEY: misc_feature
     113 <222> LOCATION: (2)..(3)
     114 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
     117 <220> FEATURE:
     118 <221> NAME/KEY: misc_feature
     119 <222> LOCATION: (13)..(14)
     120 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
     123 <220> FEATURE:
     124 <221> NAME/KEY: misc_feature
     125 <222> LOCATION: (15)..(15)
     126 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
     129 <220> FEATURE:
     130 <221> NAME/KEY: misc_feature
     131 <222> LOCATION: (16)..(16)
     132 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
     135 <220> FEATURE:
     136 <221> NAME/KEY: misc_feature
     137 <222> LOCATION: (17)..(17)
     138 <223> OTHER INFORMATION: N= 2'-O-MOE A
     141 <220> FEATURE:
     142 <221> NAME/KEY: misc_feature
     143 <222> LOCATION: (18)..(19)
```

RAW SEQUENCE LISTING          DATE: 12/06/2001
PATENT APPLICATION:  US/09/996,292     TIME: 11:33:45

Input Set : A:\ISIS4804.ST25.txt
Output Set: N:\CRF3\12062001\I996292.raw

```
        144 <223> OTHER INFORMATION: N= 2'-O-MOE G
        147 <220> FEATURE:
        148 <221> NAME/KEY: misc_feature
        149 <222> LOCATION: (20)..(20)
        150 <223> OTHER INFORMATION: N= L-Thymidine
        153 <400> SEQUENCE: 3                                         20
W--> 154 nnngtcatcg ctnnnnnnnn
        157 <210> SEQ ID NO: 4
        158 <211> LENGTH: 20
        159 <212> TYPE: DNA
        160 <213> ORGANISM: Artificial Sequence
        162 <220> FEATURE:
        163 <223> OTHER INFORMATION: Novel Sequence
        165 <220> FEATURE:
        166 <221> NAME/KEY: misc_feature
        167 <222> LOCATION: (1)..(20)
        168 <223> OTHER INFORMATION: All P=S
        171 <400> SEQUENCE: 4                                         20
        172 tgcatccccc aggccaccat
        175 <210> SEQ ID NO: 5
        176 <211> LENGTH: 20
        177 <212> TYPE: DNA
        178 <213> ORGANISM: Artificial Sequence
        180 <220> FEATURE:
        181 <223> OTHER INFORMATION: Novel Sequence
        183 <220> FEATURE:
        184 <221> NAME/KEY: misc_feature
        185 <222> LOCATION: (1)..(20)
        186 <223> OTHER INFORMATION: All P=S
        189 <220> FEATURE:
        190 <221> NAME/KEY: misc_feature
        191 <222> LOCATION: (1)..(1)
        192 <223> OTHER INFORMATION: N= L-Thymidine
        195 <220> FEATURE:
        196 <221> NAME/KEY: misc_feature
        197 <222> LOCATION: (20)..(20)
        198 <223> OTHER INFORMATION: N= L-Thymidine
        201 <400> SEQUENCE: 5                                         20
W--> 202 ngcatccccc aggccaccan
        205 <210> SEQ ID NO: 6
        206 <211> LENGTH: 17
        207 <212> TYPE: DNA
        208 <213> ORGANISM: Artificial Sequence
        210 <220> FEATURE:
        211 <223> OTHER INFORMATION: Novel Sequence
        213 <220> FEATURE:
        214 <221> NAME/KEY: misc_feature
        215 <222> LOCATION: (1)..(17)
        216 <223> OTHER INFORMATION: All P=S
```

RAW SEQUENCE LISTING                    DATE: 12/06/2001
PATENT APPLICATION:  US/09/996,292      TIME: 11:33:45

Input Set : A:\ISIS4804.ST25.txt
Output Set: N:\CRF3\12062001\I996292.raw

```
219 <400> SEQUENCE: 6
220 tcccgctgtg atgcatt                                               17
223 <210> SEQ ID NO: 7
224 <211> LENGTH: 17
225 <212> TYPE: DNA
226 <213> ORGANISM: Artificial Sequence
228 <220> FEATURE:
229 <223> OTHER INFORMATION: Novel Sequence
231 <220> FEATURE:
232 <221> NAME/KEY: misc_feature
233 <222> LOCATION: (1)..(17)
234 <223> OTHER INFORMATION: All P=S
237 <220> FEATURE:
238 <221> NAME/KEY: misc_feature
239 <222> LOCATION: (1)..(1)
240 <223> OTHER INFORMATION: N= L-Thymidine
243 <220> FEATURE:
244 <221> NAME/KEY: misc_feature
245 <222> LOCATION: (2)..(3)
246 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
249 <220> FEATURE:
250 <221> NAME/KEY: misc_feature
251 <222> LOCATION: (15)..(15)
252 <223> OTHER INFORMATION: N= 2'-O-MOE A
255 <220> FEATURE:
256 <221> NAME/KEY: misc_feature
257 <222> LOCATION: (16)..(16)
258 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
261 <220> FEATURE:
262 <221> NAME/KEY: misc_feature
263 <222> LOCATION: (17)..(17)
264 <223> OTHER INFORMATION: N= L-Thymidine
267 <400> SEQUENCE: 7
W--> 268 nnncgctgtg atgcnnn                                          17
271 <210> SEQ ID NO: 8
272 <211> LENGTH: 20
273 <212> TYPE: DNA
274 <213> ORGANISM: Artificial Sequence
276 <220> FEATURE:
277 <223> OTHER INFORMATION: Novel Sequence
279 <220> FEATURE:
280 <221> NAME/KEY: misc_feature
281 <222> LOCATION: (1)..(20)
282 <223> OTHER INFORMATION: All P=S
285 <220> FEATURE:
286 <221> NAME/KEY: misc_feature
287 <222> LOCATION: (1)..(1)
288 <223> OTHER INFORMATION: N= L-Cytidine
291 <220> FEATURE:
```

```
292 <221> NAME/KEY: misc_feature
293 <222> LOCATION: (2)..(2)
294 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
297 <220> FEATURE:
298 <221> NAME/KEY: misc_feature
299 <222> LOCATION: (3)..(3)
300 <223> OTHER INFORMATION: N= 2'-O-MOE A
303 <220> FEATURE:
304 <221> NAME/KEY: misc_feature
305 <222> LOCATION: (4)..(4)
306 <223> OTHER INFORMATION: N= 2'-O-MOE G
309 <220> FEATURE:
310 <221> NAME/KEY: misc_feature
311 <222> LOCATION: (5)..(5)
312 <223> OTHER INFORMATION: N= 2'-O-MOE A
315 <220> FEATURE:
316 <221> NAME/KEY: misc_feature
317 <222> LOCATION: (16)..(16)
318 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
321 <220> FEATURE:
322 <221> NAME/KEY: misc_feature
323 <222> LOCATION: (17)..(17)
324 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
327 <220> FEATURE:
328 <221> NAME/KEY: misc_feature
329 <222> LOCATION: (18)..(18)
330 <223> OTHER INFORMATION: N= 2'-O-MOE G
333 <220> FEATURE:
334 <221> NAME/KEY: misc_feature
335 <222> LOCATION: (19)..(19)
336 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
339 <220> FEATURE:
340 <221> NAME/KEY: misc_feature
341 <222> LOCATION: (20)..(20)
342 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
345 <400> SEQUENCE: 8
346 nnnnnttcca cactcnnnnn                                        20
349 <210> SEQ ID NO: 9
350 <211> LENGTH: 20
351 <212> TYPE: DNA
352 <213> ORGANISM: Artificial Sequence
354 <220> FEATURE:
355 <223> OTHER INFORMATION: Novel Sequence
357 <220> FEATURE:
358 <221> NAME/KEY: misc_feature
359 <222> LOCATION: (1)..(20)
360 <223> OTHER INFORMATION: All P=S
363 <220> FEATURE:
364 <221> NAME/KEY: misc_feature
```

W-->

**VERIFICATION SUMMARY**                          DATE: 12/06/2001
PATENT APPLICATION:  US/09/996,292               TIME: 11:33:46

Input Set. : **A:\ISIS4804.ST25.txt**
Output Set: **N:\CRF3\12062001\I996292.raw**


L:9 M:270 C: Current Application Number differs, Replaced Current Application No
L:9 M:271 C: Current Filing Date differs, Replaced Current Filing Date
L:40 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1
L:88 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2
L:154 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3
L:202 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:5
L:268 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:7
L:346 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:8
L:424 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:9
L:502 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10
L:568 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:11
L:640 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:12
L:688 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:13
L:736 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:14
L:790 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:15
L:868 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:16
L:934 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:17
L:1012 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:18
L:1078 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:19
L:1156 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:20
L:1234 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:21
L:1312 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:22
L:1396 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:23
L:1462 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:24
L:1534 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:25
L:1613 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:26
L:1693 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:27
L:1772 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:28
L:1852 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:29
L:1930 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:30
L:2008 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:31
L:2086 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:32
L:2166 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:33
L:2184 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:34
L:2202 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:35
L:2220 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:36
L:2238 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:37
L:2262 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:38
L:2286 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:39
L:2322 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:41
L:2364 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:43
L:2388 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:44
L:2412 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:45
L:2436 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:46
L:2460 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:47
L:2484 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:48
L:2508 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:49
L:2538 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:51

VERIFICATION SUMMARY                    DATE: 12/06/2001
PATENT APPLICATION:  US/09/996,292      TIME: 11:33:46

Input Set : A:\ISIS4804.ST25.txt
Output Set: N:\CRF3\12062001\I996292.raw

```
L:2556 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:52
L:2580 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:53
L:2598 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:54
L:2616 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:55
```